

AMENDMENTS TO THE CLAIMS

The following listing of claims will replace all prior versions and listings of claims in the application.

Listing of Claims:

1. (Currently Amended) A pneumococcus type 5 capsular polysaccharide which is aminated on the terminal aldehyde group and which exhibits (i) no resonance signal between 13 and 14 ppm inclusive in a carbon (¹³C) NMR spectrum—~~lacking a resonance signal between 13 and 14 ppm inclusive~~; (ii) no peak between fucosamine and pneumosamine peaks in an HPAEC-PAD chromatogram obtained by elution from a CarboPacTM PA10 anion-exchange column in an 18 mM sodium hydroxide solution at a flow rate of 1 ml/min for 15 min of monosaccharides derived from hydrolysis of said polysaccharide; ~~wherein said chromatogram lacks a peak between fucosamine and pneumosamine peaks~~; or (iii) both,

wherein the anion-exchange column consists of a support based on polystyrene and sulfonated divinylbenzene having a degree of cross-linking of 55% and latex microbeads with quaternary ammonium groups; wherein the latex microbeads have a degree of cross-linking of 5% and the diameter of 400 nm.

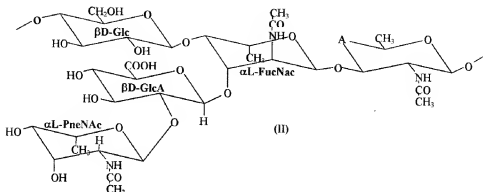
2. (Original) The polysaccharide according to Claim 1, which exhibits:
 - (i) a carbon NMR spectrum which comprises a resonance signal between 11.5 and 12.5 ppm, inclusive, characteristic of a Sug compound, and a resonance signal located between 17 and 18 ppm inclusive, characteristic of N-acetylated quinovosamine, the intensity of which is less in comparison with the resonance signal located between 17 and 18 ppm, inclusive, in the (¹³C) NMR spectrum of a pneumococcus type 5 capsular polysaccharide obtained after reductive amination in the presence of sodium cyanoborohydride at pH 8 for 48 hours; or
 - (ii) an HPAEC-PAD chromatogram obtained under the conditions specified in Claim 1, which comprises a peak located immediately after the pneumosamine peak, characteristic of quinovosamine, the intensity of which is less in comparison with

the equivalent peak in the HPAEC-PAD chromatogram of a pneumococcus type 5 capsular polysaccharide obtained after reductive amination in the presence of sodium cyanoborohydride at pH 8 for 48 hours; or

(iii) both.

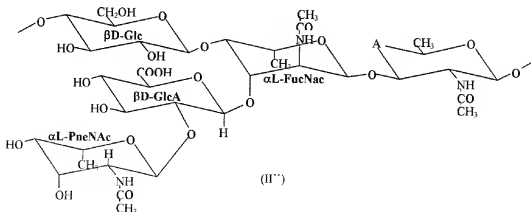
3. (Currently Amended) The polysaccharide according to Claim 1 which exhibits (i) ~~no resonance signal between 17 and 18 ppm in a carbon NMR spectrum entirely lacking a resonance signal between 17 and 18 ppm~~; (ii) ~~no quinovosamine peak in an HPAEC-PAD chromatogram obtained according to the conditions of claim 1 lacking a quinovosamine peak~~, the peak observed with the polysaccharide aminated according to a conventional amination method being reduced so as to be no more than a simple shoulder of the preceding peak (pneumosamine peak); or (iii) both.
4. (Original) The aminated polysaccharide according to Claim 1, which exhibits:
 - (i) a carbon NMR spectrum lacking a resonance signal between 11.5 and 12.5 ppm, inclusive, characteristic of a Sug compound, which comprises a resonance signal located between 17 and 18 ppm inclusive, characteristic of N-acetylated quinovosamine, the intensity of which is increased in comparison with the resonance signal located between 17 and 18 ppm, inclusive, in the (¹³C) NMR spectrum of a pneumococcus type 5 capsular polysaccharide obtained after reductive amination in the presence of sodium cyanoborohydride at pH 8 for 48 hours; or
 - (ii) an HPAEC-PAD chromatogram obtained under the specified in Claim 1 which comprises a peak located immediately after the pneumosamine peak, characteristic of quinovosamine, the intensity of which is increased in comparison with the equivalent peak in the HPAEC-PAD chromatogram of a pneumococcus type 5 capsular polysaccharide obtained after reductive amination in the presence of sodium cyanoborohydride at pH 8 for 48 hours; or
 - (iii) both.

5. (Original) A pneumococcus type 5 capsular polysaccharide which is aminated on the terminal aldehyde group, consisting of repeating units, at least 85% of the repeating units of which correspond to formula (II)



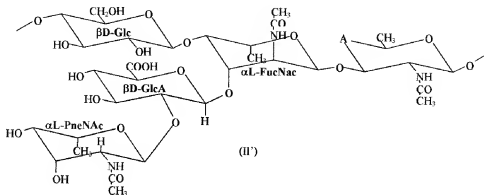
in which A is independently and randomly C=O or CHOH.

6. (Original) The polysaccharide according to Claim 5 in which at least 90% of the repeating units correspond to formula (II).
7. (Original) The polysaccharide according to Claim 6 in which at least 95% of the repeating units correspond to formula (II).
8. (Original) The polysaccharide according to Claim 5 in which at least 95% of the repeating units corresponding to formula (II) correspond to formula II''



in which A is CHOH.

9. (Original) The polysaccharide according to Claim 5 in which 85 to 95% of the repeating units corresponding to formula (II) correspond to formula II'



in which A is C=O.

10. (Original) The conjugate in which a polysaccharide according to Claim 1 is coupled to a carrier polypeptide (P).
11. (Withdrawn) A method for producing an aminated pneumococcus type 5 capsular polysaccharide, wherein the polysaccharide is subjected to a reductive amination in the presence of a reducing agent selective for a Schiff base at a pH of 4 to 6.5 for a period not exceeding 4 hours.
12. (Withdrawn) The method according to Claim 11 in which the polysaccharide is subjected to a reductive amination at a pH of 5 to 6.
13. (Withdrawn) The method according to Claim 11 in which the polysaccharide is subjected to a reductive amination for a period not exceeding 2 hours.
14. (Withdrawn) The method according to Claim 11 in which the reducing agent selective for a Schiff base is cyanoborohydride or pyridine borane complex.
15. (Withdrawn) A method for producing an aminated pneumococcus type 5 capsular polysaccharide, according to which (i) the polysaccharide is reacted with an agent for reducing a ketone function, (ii) the reduced polysaccharide is fragmented, and (iii) the reduced and fragmented polysaccharide is subjected to a reductive amination.

16. (Withdrawn) The method according to Claim 15 in which the polysaccharide which is reacted with the agent capable of reducing a ketone function is in native form.
17. (Withdrawn) The method according to Claim 15 in which the agent capable of reducing a ketone function is NaBH_4 .
18. (Withdrawn) The method according to Claim 15 in which the reduced polysaccharide is fragmented by oxidative free-radical depolymerization.
19. (Withdrawn) A method for producing a conjugate of formula $\text{Ps-CH}_2\text{-NH-P}$, according to which a method according to Claim 11 is used, wherein the pneumococcus type 5 capsular polysaccharide (Ps) is coupled by reductive amination to a carrier polypeptide (P) in the presence of a reducing agent selective for a Schiff base at a pH of 4 to 6.5 for a period not exceeding 4 hours.
20. (Withdrawn) A method for producing a conjugate of formula $\text{Ps-CH}_2\text{-NH-P}$, according to which a method according to Claim 15 is used, in which the reduced and fragmented pneumococcus type 5 capsular polysaccharide (Ps) is coupled by reductive amination with a carrier polypeptide (P).
21. (Withdrawn) A method for producing a conjugate of formula $\text{Ps-CH}_2\text{-NH-L-P}$, according to which:
 - (i) the method according to Claim 11 is used, wherein the pneumococcus type 5 capsular polysaccharide (Ps) is coupled by reductive amination to a linking agent (L) having at least one free amine function so as to form an aminated and activated polysaccharide of formula $\text{Ps-CH}_2\text{-NH-L}$, and the activated polysaccharide is coupled to a carrier polypeptide (P) in order to obtain the conjugate of formula $\text{Ps-CH}_2\text{-NH-L-P}$; or, alternatively,
 - (ii) the method according to Claim 11 is used, wherein the pneumococcus type 5 capsular polysaccharide (Ps) is coupled by reductive amination to an activated carrier polypeptide of formula L-P, wherein L is a linking agent having at least one free amine function, in order to obtain the conjugate of formula $\text{Ps-CH}_2\text{-NH-L-P}$.

22. (Withdrawn) A method for producing a conjugate of formula $\text{Ps-CH}_2\text{-NH-L-P}$, in which:
- (i) (a) a method according to Claim 15 is used, wherein the reduced and fragmented pneumococcus type 5 capsular polysaccharide (Ps) is coupled by reductive amination to a linking agent (L) having at least one free amine function so as to form an aminated and activated polysaccharide of formula $\text{Ps-CH}_2\text{-NH-L}$, and
 - (b) the activated polysaccharide is coupled to a carrier polypeptide (P) in order to obtain the conjugate of formula $\text{Ps-CH}_2\text{-NH-L-P}$; or, alternatively,
 - (ii) the method according to Claim 15 is used, wherein the reduced and fragmented pneumococcus type 5 capsular polysaccharide (Ps) is coupled by reductive amination to an activated carrier polypeptide of formula L-P , wherein L is a linking agent having at least one free amine function, in order to obtain the conjugate of formula $\text{Ps-CH}_2\text{-NH-L-P}$.
23. (Withdrawn) A method for producing a conjugate of formula $\text{Ps-CH}_2\text{-NH-S-L'-P}$, in which:
- (i) the method according to Claim 11 is used, wherein the pneumococcus type 5 capsular polysaccharide (Ps) is coupled by reductive amination to a spacer (S) having at least one free amine function, so as to form an aminated and derivatized polysaccharide of formula $\text{Ps-CH}_2\text{-NH-S}$, and
 - (ii) (a) the derivatized polysaccharide is coupled with a linking agent (L'), in order to obtain an activated polysaccharide of formula $\text{Ps-CH}_2\text{-NH-S-L'}$, then the activated polysaccharide is coupled with a carrier polypeptide (P), in order to obtain the conjugate of formula $\text{Ps-CH}_2\text{-NH-S-L'-P}$; or, alternatively,
 - (b) the derivatized polysaccharide is coupled with an activated carrier polypeptide of formula L'-P , in which L' is a linking agent, in order to obtain the conjugate of formula $\text{Ps-CH}_2\text{-NH-S-L'-P}$.
24. (Withdrawn) A method for producing a conjugate of formula $\text{Ps-CH}_2\text{-NH-S-L'-P}$, in which:
- (i) the method according to Claim 15 is used, wherein the reduced and fragmented pneumococcus type 5 capsular polysaccharide (Ps) is coupled by reductive

amination to a spacer (S) having at least one free amine function so as to form an aminated and derivatized polysaccharide of formula $\text{Ps-CH}_2\text{-NH-S}$, and

- (ii) (a) the derivatized polysaccharide is coupled with a linking agent (L') in order to obtain an activated polysaccharide of formula $\text{Ps-CH}_2\text{-NH-S-L}'$, then the activated polysaccharide is coupled with a carrier polypeptide (P), in order to obtain the conjugate of formula $\text{Ps-CH}_2\text{-NH-S-L}'\text{-P}$; or, alternatively,
 - (b) the derivatized polysaccharide is coupled with an activated carrier polypeptide of formula $\text{L}'\text{-P}$, wherein L' is a linking agent, in order to obtain the conjugate of formula $\text{Ps-CH}_2\text{-NH-S-L}'\text{-P}$.
25. (Withdrawn) The method according to Claim 19, wherein the carrier polypeptide P is diphtheria toxoid or tetanus toxoid.
26. (Withdrawn) The method according to Claim 21, wherein the linking agent (L) is a compound of formula (XII) R1-A-R2 , in which:
A denotes an aliphatic or aromatic chain or a mixed aliphatic and aromatic chain, which may be substituted or unsubstituted;
R1 denotes a primary amine or a chemical radical carrying a primary amine; and
R2 denotes a functional group capable of reacting with a carbonyl, thiol or amine group.
27. (Withdrawn) The method according to Claim 26, wherein the linking agent (L) is an alkyl dihydrazide or a diaminoalkyl.
28. (Withdrawn) The method according to Claim 23, wherein the spacer S is an aminothiols and the linking agent L' is a succinimidylmaleimidylalkyl.
29. (Withdrawn) The method according to Claim 23, wherein the spacer S is a diaminoalkyl or a dihydrazide, and the linking agent L' is chosen from disuccinimidylalkyl or succinimidylmaleimidoalkyl compounds of formula (XIV) R3-B-R4 in which B is an alkyl group, R3 is a succinimidyl group and R4 is a succinimidyl or maleimido group.
30. (Original) A pharmaceutical composition comprising a conjugate according to Claim 10.
31. (Currently Amended) A pharmaceutical composition comprising a conjugate obtained ~~using the method according to Claim 19~~ by subjecting a pneumococcus type 5 capsular

polysaccharide to a reductive amination in the presence of a reducing agent selective for a Schiff base at a pH of 4 to 6.5 for a period not exceeding 4 hours, wherein the pneumococcus type 5 capsular polysaccharide (Ps) is coupled by the reductive amination to a carrier polypeptide (P).